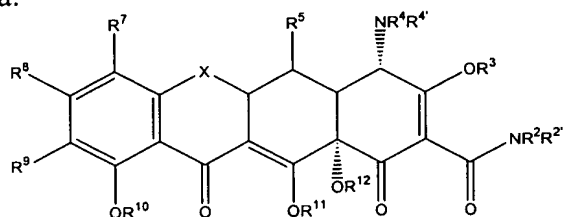


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of the claims and listings of the claims in the application:

1. **(Currently Amended)** A substituted tetracycline compound, wherein said compound is of the formula:



(I)

wherein:

X is CHC(R¹³Y'Y), CR^{6'}R⁶, S, NR⁶, or O;

R² is hydrogen, alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ and R^{4'} are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{2'}, R³, R¹⁰, R¹¹ and R¹² are each hydrogen or a pro-drug moiety;

R⁵ is hydrogen, hydroxyl, or a prodrug moiety;

R⁶, R^{6'}, and R⁸ are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, or halogen;

R⁷ is hydrogen, dialkylamino, ~~heteroaryl-amino~~, or NR^{7c}C(=W')WR^{7a};

R⁸ is hydrogen;

R¹³ is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino; or an arylalkyl;

Y' and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

R⁹ is hydrogen, or NR^{9c}C(=Z')ZR^{9a}, ~~or heteroaryl-amino~~;

Z is CR^{9d}R^{9e}, NR^{9b}, ~~or~~ O;

Z' is O or S;

R^{9a} ~~is~~, R^{9d}, and R^{9e} ~~are each independently ethyl, t-butyl, n-butyl, i-butyl, or n-pentyl, substituted alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl,~~

alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, a steroid, absent, or a prodrug moiety, ~~and R^{9d} and R^{9e} may be linked to form a ring;~~

~~R^{9b} and R^{9c} is are each independently~~ hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic or heteroaromatic;

W is CR^{7d}R^{7e}, NR^{7b} or O;

W' is O or S; and

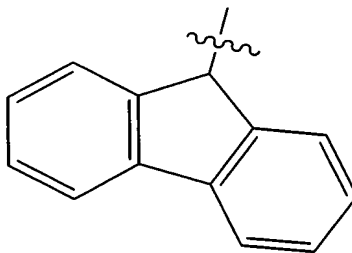
R^{7a}, R^{7b}, R^{7c}, R^{7d}, and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, absent, or a prodrug moiety, and R^{7d} and R^{7e} may be linked to form a ring;

and pharmaceutically acceptable salts thereof, provided that at least one of R⁹ is not hydrogen when R⁷ is hydrogen or dialkylamino.

2. **(Original)** The compound of claim 1, wherein R², R^{2'}, R³, R⁸, R¹⁰, R¹¹, and R¹² are each hydrogen.
3. **(Original)** The compound of claim 2, wherein R⁴ and R^{4'} are each alkyl.
4. **(Original)** The compound of claim 3, wherein R⁴ and R^{4'} are each methyl
5. **(Cancelled)**
6. **(Original)** The compound of claim 4, wherein R⁵ is hydrogen.
7. **(Original)** The compound of claim 6, wherein X is CH₂, and R⁷ is hydrogen.
8. **(Original)** The compound of claim 6, wherein X is CH₂, and R⁷ is N(Me)₂.
9. **(Original)** The compound of claim 4, wherein R⁵ is hydroxyl or a prodrug moiety, and X is CHR⁶.
10. **(Original)** The compound of claim 9, wherein R⁵ is hydroxyl and R⁶ is CH₃.
11. **(Original)** The compound of claim 1, wherein R⁹ is NR^{9c}C(=Z')ZR^{9a}.

12. **(Original)** The compound of claim 11, wherein R^{9c} is hydrogen.
13. **(Original)** The compound of claim 11, wherein Z' is oxygen.
14. **(Original)** The compound of claim 11, wherein Z' is sulfur.
15. **(Cancelled)**
16. **(Original)** The compound of claim 13 or 14, wherein Z is oxygen.
17. **(Cancelled)**
18. **(Cancelled)**
19. **(Currently Amended)** The compound of claim 11, wherein R^{9a} is selected from the group consisting of ~~ethyl, t-butyl, n-butyl, i-butyl, or n-pentyl~~, substituted alkyl, ~~alkenyl~~, alkynyl, aryl, arylalkyl, or heteroaromatic, ~~and multicyclic~~.
20. **(Cancelled)**
21. **(Currently Amended)** The compound of claim ~~20~~ 19, wherein R^{9a} said substituted alkyl is substituted with one or more substituents selected from the group consisting of alkoxy, carbonyl, amino, aryl, carbonyl, halogen, hydroxy, alkylamino, alkoxy, or aryl.
22. **(Cancelled)**
23. **(Currently Amended)** The compound of claim 19, wherein said ~~ethyl, t-butyl, n-butyl, i-butyl, or n-pentyl~~ substituted alkyl is substituted with an aryl group.
24. **(Original)** The compound of claim 23, wherein said aryl group is phenyl.
25. **(Currently Amended)** The compound of claim 19, wherein said ~~ethyl, t-butyl, n-butyl, i-butyl, or n-pentyl~~ said substituted alkyl is substituted with one or more halogens.

26. **(Original)** The compound of claim 24, wherein said halogen is bromine.
27. **(Cancelled)**
28. **(Currently Amended)** The compound of claim 27 1, wherein R^{9a} is a steroid.
29. **(Original)** The compound of claim 28, wherein R^{9a} is cholesterol.
30. **(Original)** The compound of claim 19, wherein R^{9a} is substituted or unsubstituted aryl.
31. **(Original)** The compound of claim 30, wherein said substituted or unsubstituted aryl is naphthyl.
32. **(Original)** The compound of claim 30, wherein said substituted or unsubstituted aryl is of the formula:



33. **(Original)** The compound of claim 30, wherein said substituted or unsubstituted aryl is phenyl.
34. **(Original)** The compound of claim 33, wherein said aryl is substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, amido, halogen, nitro, azo, alkyl sulfonyl, and arylsulfonyl.
35. **(Original)** The compound of claim 34, wherein said substituent is alkyl.
36. **(Original)** The compound of claim 35, wherein said alkyl is unsubstituted.

37. **(Original)** The compound of claim 35, wherein said alkyl is methyl.
38. **(Original)** The compound of claim 35, wherein said alkyl is substituted with one or more halogens.
39. **(Original)** The compound of claim 34, wherein said substituent is methoxy.
40. **(Original)** The compound of claim 34, wherein said substituent is selected from the group consisting of alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy carbonyl, and amido.
- 41-55. **(Cancelled)**
56. **(Original)** The compound of claim 1, wherein R^7 is $NR^{7c}C(=W')WR^{7a}$.
57. **(Original)** The compound of claim 56, wherein R^9 is hydrogen.
58. **(Original)** The compound of claim 57, wherein R^{7c} is hydrogen.
59. **(Original)** The compound of claim 57, wherein W' is oxygen.
60. **(Original)** The compound of claim 57, wherein W' is sulfur
61. **(Original)** The compound of claims 59 or 60, wherein W is NR^{7b} .
62. **(Original)** The compound of claims 59 or 60, wherein W is oxygen.
63. **(Currently Amended)** The compound of claim 57, wherein R^{7a} is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, and heteroaromatic, ~~and~~ ~~multicyclic~~.
64. **(Original)** The compound of claim 63, wherein R^{7a} is substituted or unsubstituted alkyl.
65. **(Original)** The compound of claim 64, wherein said alkyl is substituted with an aryl group.

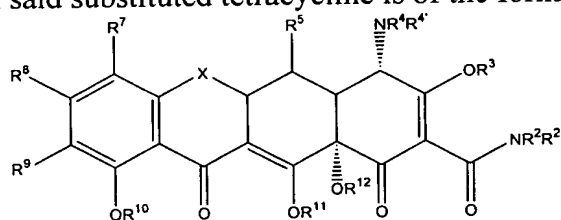
66. **(Original)** The compound of claim 63, wherein said substituted or unsubstituted aryl is phenyl.

67. **(Original)** The compound of claim 66, wherein said aryl is substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, amido, halogen, nitro, azo, alkyl sulfonyl, and arylsulfonyl.

68. **(Original)** The compound of claim 67, wherein said substituent is alkyl, alkoxy, or nitro.

Claims 69.-81. **(Cancelled)**

82. **(Currently Amended)** A pharmaceutical composition comprising a therapeutically effective amount of a substituted tetracycline compound and a pharmaceutically acceptable carrier, wherein said substituted tetracycline is of the formula:



(I)

wherein:

X is CHC(R¹³Y'Y), CR⁶R⁶, S, NR⁶, or O;

R² is hydrogen, alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R⁴ and R^{4'} are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{2'}, R³, R¹⁰, R¹¹ and R¹² are each hydrogen or a pro-drug moiety;

R⁵ is hydrogen, hydroxyl, or a prodrug moiety;

R⁶, R^{6'}, and R⁸ are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, or halogen;

R⁷ is hydrogen, dialkylamino, ~~heteroaryl-amino~~, or NR^{7c}C(=W')WR^{7a};

R⁸ is hydrogen;

R^{13} is hydrogen, hydroxy, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

Y' and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

R^9 is hydrogen; ~~or $NR^{9c}C(=Z')ZR^{9a}$, or heteroaryl-amino;~~

Z is ~~$CR^{9d}R^{9e}$, NR^{9b} , or O ;~~

Z' is O or S ;

~~R^{9a} , R^{9d} , and R^{9e} are each independently ethyl, t-butyl, n-butyl, i-butyl, or n-pentyl, is substituted alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, a steroid, absent, or a prodrug moiety, and R^{9d} and R^{9e} may be linked to form a ring;~~

~~R^{9b} and R^{9c} is~~ are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic or heteroaromatic;

W is $CR^{7d}R^{7e}$, NR^{7b} or O ;

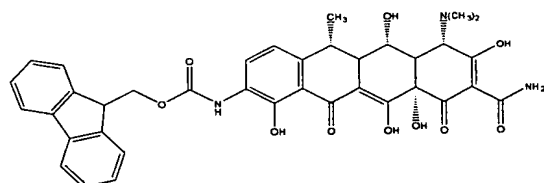
W' is O or S ; and

R^{7a} , R^{7b} , R^{7c} , R^{7d} , and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, absent, or a prodrug moiety, and R^{7d} and R^{7e} may be linked to form a ring;

and pharmaceutically acceptable salts thereof, provided that R^9 is not hydrogen, when R^7 is dialkylamino or hydrogen.

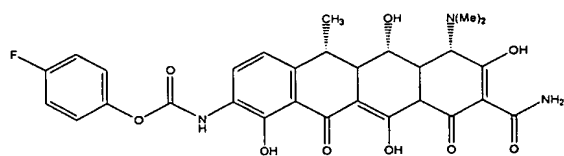
83.-102. (Cancelled)

103. (New) The compound of claim 1, wherein said compound is



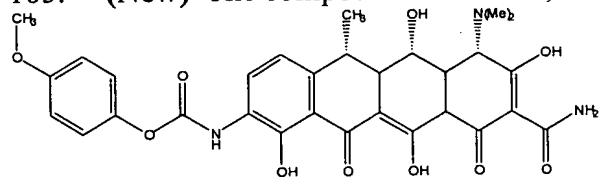
and pharmaceutically acceptable salts and prodrugs thereof.

104. (New) The compound of claim 1, wherein said compound is



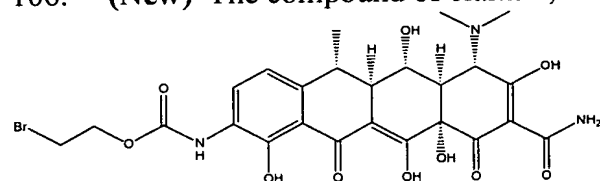
and pharmaceutically acceptable salts and prodrugs thereof.

105. (New) The compound of claim 1, wherein said compound is



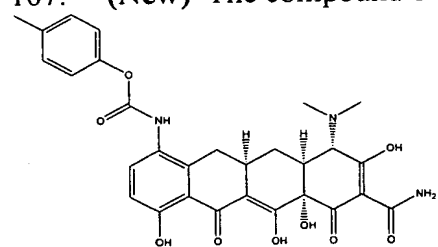
and pharmaceutically acceptable salts and prodrugs thereof.

106. (New) The compound of claim 1, wherein said compound is



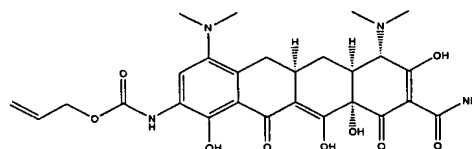
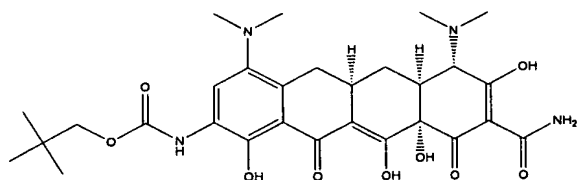
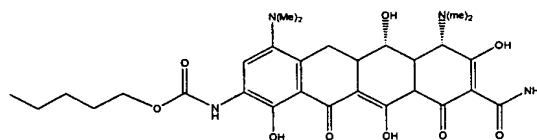
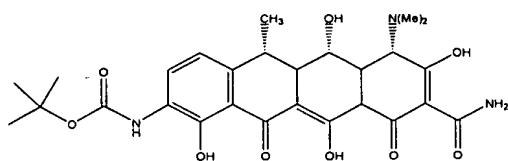
and pharmaceutically acceptable salts and prodrugs thereof.

107. (New) The compound of claim 1, wherein said compound is



and pharmaceutically acceptable salts and prodrugs thereof.

108. (New) A substituted tetracycline compound, wherein said compound is selected from the group consisting of



and

and pharmaceutically acceptable salts and prodrugs thereof.

109. **(New)** The compound of claim 1, wherein said compound is doxycycline 9-carbamic acid 9*H*-fluoren-9-yl methyl ester and pharmaceutically acceptable salts and prodrugs thereof.

110. **(New)** The compound of claim 1, wherein said compound is Fmoc 9-amino doxycycline and pharmaceutically acceptable salts and prodrugs thereof.

111. **(New)** The compound of claim 1, wherein said compound is 9-(4'-fluorophenyl) doxycycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

112. **(New)** The compound of claim 1, wherein said compound is 9-(4'-methoxyphenyl) doxycycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

113. **(New)** The compound of claim 1, wherein said compound is minocycline 9-carbamic acid 9*H*-fluoren-9-yl methyl ester and pharmaceutically acceptable salts and prodrugs thereof.

114. **(New)** The compound of claim 1, wherein said compound is Fmoc 9-amino minocycline and pharmaceutically acceptable salts and prodrugs thereof.

115. **(New)** The compound of claim 1, wherein said compound is 9-(4'-fluorophenyl) minocycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

116. **(New)** The compound of claim 1, wherein said compound is 9-(4'-Methoxyphenyl) minocycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

117. **(New)** The compound of claim 1, wherein said compound is 9-(2'-bromoethyl) doxycycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

118. **(New)** The compound of claim 1, wherein said compound is 7-(4'-methylphenyl) sancycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

119. **(New)** The compound of claim 1, wherein said compound is doxycycline 7-carbamic acid 7*H*-fluoren-7-yl methyl ester and pharmaceutically acceptable salts and prodrugs thereof.

120. **(New)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline urea and pharmaceutically acceptable salts and prodrugs thereof.

121. **(New)** The compound of claim 1, wherein said compound is 7-(3-methyl-1-butyl) doxycycline urea and pharmaceutically acceptable salts and prodrugs thereof.

122. **(New)** The compound of claim 1, wherein said compound is 7-phenyl doxycycline urea and pharmaceutically acceptable salts and prodrugs thereof.

123. **(New)** The compound of claim 1, wherein said compound is 7-*t*-butyl doxycycline urea and pharmaceutically acceptable salts and prodrugs thereof.

124. **(New)** The compound of claim 1, wherein said compound is 7-Fmoc amino doxycycline and pharmaceutically acceptable salts and prodrugs thereof.

125. **(New)** The compound of claim 1, wherein said compound is 7-(4'-chloro-2-trifluoromethylphenyl) doxycycline urea and pharmaceutically acceptable salts and prodrugs thereof.

126. **(New)** The compound of claim 1, wherein said compound is 7-(4'-fluorophenyl) doxycycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

127. **(New)** The compound of claim 1, wherein said compound is 7-(4'-methoxyphenyl) doxycycline carbamate and pharmaceutically acceptable salts and prodrugs thereof.

128. **(New)** The compound of claim 1, wherein said compound is 7-BOC amino doxycycline and pharmaceutically acceptable salts and prodrugs thereof.
129. **(New)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline thiourea 5-propanoic acid ester and pharmaceutically acceptable salts and prodrugs thereof.
130. **(New)** The compound of claim 1, wherein said compound is doxycycline 7-thiocarbamic acid 7H-fluoren-7-yl methyl ester and pharmaceutically acceptable salts and prodrugs thereof.
131. **(New)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline thiourea and pharmaceutically acceptable salts and prodrugs thereof.
132. **(New)** The compound of claim 1, wherein said compound is 7-(3-methyl-1-butyl) doxycycline thiourea and pharmaceutically acceptable salts and prodrugs thereof.
133. **(New)** The compound of claim 1, wherein said compound is 7-phenyl amino doxycycline thiourea and pharmaceutically acceptable salts and prodrugs thereof.
134. **(New)** The compound of claim 1, wherein said compound is 7-t-butyl amino doxycycline thiourea and pharmaceutically acceptable salts and prodrugs thereof.
135. **(New)** The compound of claim 1, wherein said compound is 7-(4'-chloro-2'-trifluoromethylphenyl) doxycycline thiourea and pharmaceutically acceptable salts and prodrugs thereof.
136. **(New)** The compound of claim 1, wherein said compound is 7-(4'-fluorophenyl) doxycycline thiocarbamate and pharmaceutically acceptable salts and prodrugs thereof.
137. **(New)** The compound of claim 1, wherein said compound is 7-(4'-methoxyphenyl) doxycycline thiocarbamate and pharmaceutically acceptable salts and prodrugs thereof.
138. **(New)** The compound of claim 1, wherein said compound is 7-(naphthyn-1-yl) doxycycline urea 5-propanoic acid ester and pharmaceutically acceptable salts and prodrugs thereof.

139. (New) A substituted tetracycline compound, wherein said compound is selected from the group consisting of:

9-neopentyl minocycline carbamate;

9-BOC amino doxycycline;

9-(n-pentyl) minocycline carbamate;

9-BOC amino minocycline carbamate;

9-(n-pentyl) minocycline carbamate;

9-prop-2'-enyl minocycline carbamate;

9-ethyl minocycline carbamate;

9-n-butyl minocycline carbamate

9-n-but-3-enyl minocycline carbamate; and

9-i-butyl minocycline carbamate; and pharmaceutically acceptable salts and prodrugs thereof.